REMARKS

This Response is submitted in reply to the final Office Action mailed on May 31, 2007. No fee is due in connection with this Response. The Director is authorized to charge any fees that may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112713-983 on the account statement.

Claims 1-21 and 23-53 are currently pending in this application. Claims 22 and 54-120 were previously canceled. In the Office Action, Claims 1-21 and 23-53 are rejected under 35 U.S.C. §103. For at least the reasons set forth below, Applicants respectfully submit that the rejections should be withdrawn.

Claims 1-21, 23-34, and 48-53 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,935,847 to Smith et al. ("*Smith*") in view of U.S. Patent No. 6,759,245 to Toner et al. ("*Toner*"). Claims 36-46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Smith* and *Toner* and in further view of U.S. Patent No. 5,989,215 to Delmotte ("*Delmotte*"). Applicants respectfully disagree with and traverse these alleged rejections for at least the reasons set forth below.

Independent Claims 1, 48 and 51 recite, in part, a closed supporting container comprising a first flexible exterior side wall connected to a portion of an opposing second flexible exterior side wall and a fibrin matrix layer on a portion of the interior surface of the first side wall or the second side wall of the supporting container. An advantage of the closed supporting container is that the materials and structure of the overall container provide numerous alternatives and choices for achieving the appropriate physical properties such as gas permeabilities and flexibility to meet the various requirements of specific cells. For example, by independently varying the characteristics of the fibrin matrix and gas permeability of the container material, cell culture conditions can be optimized for a variety of cell lines. In contrast, Applicants respectfully submit that the skilled artisan would not combine the cited references to arrive at the present claims and, even if combinable, the cited references fail to disclose or suggest every element of the present claims.

Applicants respectfully submit that references must be considered as a whole and those portions teaching against or away from each other and/or the claimed invention must be

considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant." *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

Applicants respectfully submit that the skilled artisan would not combine the cited references to arrive at the claimed invention because the cited references are directed to devices having different modes of operation. For example, *Toner* is entirely directed to a modular cell culturing device including one or more two-compartment cartridges. See, *Toner*, column 2, lines 35-50. A polymeric membrane 30 (which may be coated with fibrin) separates a liquid compartment and an oxygenated fluid compartment of the cartridge. The cartridge entirely comprises rigid and impermeable exterior walls 50, which explicitly teaches away from the present claims. See, *Toner*, column 2, lines 39-45, column 7, lines 38-59, column 11, lines 27-41 ("rigid impermeable walls 50"). In fact, the walls of the cartridges are specifically intended and designed for being impermeable to liquids and gases to adequately maintain the bioreactor. See, *Toner*, column 7, lines 54-63.

Although *Toner* teaches using fibrin as a coating matter, the Patent Office's reliance on one aspect of *Toner*, which is already known in the art, while ignoring other teaching away aspects of *Toner* is a strong indication that the Patent Office is using Applicants' disclosure as a blueprint to pick and choose from isolated portions of the prior art in order to deprecate Applicants' claims. Such conduct is exemplary of hindsighted reasoning, which is clearly improper. Moreover, *Toner's* use of fibrin is specific to his device. For example, *Toner* does not coat the exterior rigid walls, but the intermediate separating membrane within the cartridge. As a result, the cells growth takes place on the intermediate membrane and not on the interior of the outer walls.

Smith is entirely directed to a multi-layer, flexible, gas-permeable container. See, *Smith*, column 2, lines 24-32. In fact, the outer walls that make up the container of *Smith* are made of the flexible, gas-permeable materials. *Smith* teaches that any cell growth takes place on the interior first and second flexible side walls. See, *Smith*, column 7, lines 7-9. Because *Smith* discloses a multi-layer flexible, gas permeable container, *Smith* explicitly teaches away from the

impermeable and rigid multi-compartment cartridge taught by *Toner*. Moreover, *Toner's* use of the intermediate membrane for cell growth would lead the skilled artisan away from using the exterior walls for cell growth as taught by *Smith*. Consequently, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Toner further teaches away from a closed container as recited in the present claims. Instead, *Toner* is entirely directed to an open or flow-through cell-culturing device. See, *Toner*, column 2, lines 35-50. *Toner's* cartridge includes oxygenated fluid inlet/out 3,3' and liquid inlet/outlet 5,5'. The inlets and outlets permit continuous fluid flow through *Toner's* cartridge. The inlets and outlets fulfill an objective of *Toner*, which is to cultivate cells on membrane 30 by passing flowing fluid along each side of the membrane 30. See, *Toner*, column 2, lines 35-45. Accordingly, *Toner's* flow-through cartridge is an open system, not a closed system. *Toner's* open, flow-through cell-culturing device therefore teaches away from the closed support container recited in the present claims.

Delmotte also teaches away from the present claims and a combination with *Smith* and *Toner*. For example, *Delmotte* teaches away from a closed support container having flexible and gas permeable exterior sidewalls in accordance with the present claims. *Delmotte* discloses a fibrin delivery device 10 having first and second syringes 12, 14 and a spray unit 18. A pressurizer 22 travels through each syringe 12, 14 to push fluid present in each syringe through the spray unit 18. *Delmotte*, col. 8 lines 31-43, col. 9 lines 47-58, Figures 1 and 4. One of ordinary skill in the art would recognize that syringes 12, 14 are rigid in order to withstand the pressure imposed by pressurizer 22 when pushing fluid out of each syringe. Moreover, *Delmotte's* rigid syringes teach away from the flexible container of *Smith* and the modular cell culturing device of *Toner*.

In addition, *Smith*, *Toner* and *Delmotte*, either alone or in combination, fail to disclose or suggest a closed support container having a fibrin matrix layer on a portion of an interior flexible sidewall surface as required, in part, by Claims 1, 48 and 51. *Smith* has no disclosure whatsoever regarding fibrin, let alone a container having a fibrin layer. In fact, the Patent Office admits the same. See, Office Action, page 3, lines 8-10. *Toner* fails to remedy the deficiencies of *Smith*. Although the Patent Office asserts that *Toner* is relied upon only for the teaching that a fibrin

matrix may be used to accommodate cell growth, Applicants respectfully submit that *Toner* is merely cumulative with respect to the knowledge that fibrin may be used as a cell growth substrate. The ability of a fibrin matrix to support cell growth is known in the art. See, specification, page 3 line 23 to page 4 line 2 (coating a polymeric material with fibrin is known in the art). As it is known in the art to use a fibrin matrix to support cell growth, the Patent Office's reliance on *Toner*'s disclosure of a fibrin matrix as a cell growth substrate is cumulative. Nevertheless, the cited references fail to even recognize the advantages, benefits and/or properties of a fibrin matrix layer on a portion of an interior flexible sidewall surface in accordance with the present claims.

In sum, *Smith* has no disclosure of a cell culture container having a fibrin layer as admitted by the Examiner. *Toner* and *Delmotte* each teach away from being combined with *Smith* and the claimed support container having flexible exterior sidewalls. For at least the reasons discussed above, the combinations of *Smith* and *Toner* or *Smith*, *Toner* and *Delmotte* are improper. Moreover, even if combinable, *Smith*, *Toner* and *Delmotte* do not teach, suggest, or even disclose all of the elements of independent Claims 1, 48 and 51 and Claims 2-21, 23-47, 49-51 and 52-53 that depend from Claims 1, 48 and 51, and thus, fail to render the claimed subject matter obvious.

Accordingly, Applicants respectfully request that the obviousness rejections with respect to Claims 1-21 and 23-53 be reconsidered and the rejections be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY _____

Robert M. Barrett
Reg. No. 30,142
Customer No. 29200

Dated: August 2, 2007